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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,122	08/08/2005	Gary A. Clawson	14017-008US1/PSU 2002-266	4883

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FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
04/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,122	CLAWSON ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-15,18-24,26-28,30-33 and 36-67* is/are pending in the application.

4a) Of the above claim(s) *8-10,18,19,30,36,37 and 40-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,11-15,20-24,26-28,31-33,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/05/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 1/08/08 in combination with the amendments filed 1/08/08 have been fully considered and are persuasive. The Milner reference has been removed as prior art due to applicants earlier effective filing date. The limitations drawn to the requirement that the nucleic acid be a double stranded RNA is sufficient to overcome the rejections of record sans Milner et al. Therefore, the rejections of record have been withdrawn. However, upon further consideration, a new ground of rejection is made below.

The examiner is including a copy of 1449 filed 6/05/06 with all references initialed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-6, 11-15, 21-24, 26-28, 31-33, 38, and 39 rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke et al [US6,174,870] and Tuschl et al [US 2004/0259247] and Li et al [US 2002/0114784].

Crooke et al have taught the use of antisense oligonucleotides to inhibit HPV16 in human cells and in humans (see claims 8-14, for example). At columns 1, and 4; and claim 14, for example, it is taught that cervical intraepithelial neoplasias as well as various other conditions are treated with antisense to HPV 16. At column 15, for example, it is disclosed to apply antisense compositions against HPV topically or interlesionally. Crooke et al do not teach the use of double stranded RNA in the treatment of HPV.

Tuschl et al have taught the use of siRNA as a universal tool for gene expression inhibition and have taught that siRNA can be used to inhibit viral genes in animal s and animal cells , including humans (see paragraphs 29 and 30 and claim 24, for example). At paragraphs 32 and 33 teach the use of pharmaceutical carriers and it is taught that siRNA can be applied by any suitable means such as by topical administration. At paragraphs 177-178 it is provided a "User Guide" for siRNA design.

Li et al have also taught siRNA can be used to treat viral infections (see paragraphs 6, 10 and 27, for example). At paragraph 44 it has bee taught that siRNA

can be administered in a plethora of known ways including topical and vaginal. It has been taught throughout Li et al that siRNA can be delivered via expression from a vector.

The prior art has therefor taught that HPV can be treated by antisense which functions to inhibit expression of HPV genes. The prior art also provides another means of nucleic acid inhibition via siRNA. Antisense and siRNA both function to inhibit a genes expression by silencing/inhibiting expression of a targeted gene. One in the art would clearly see that siRNA could easily be substituted for antisense since both function as nucleic acid inhibitors where both antisense and siRNA belong to the same class of inhibitors [small nucleic acid inhibitor] and since it was taught in the art that both can be used to inhibit viral genes.

The prior art not specifically disclose by what percent the HPV is reduced in their methods and also do not teach whether the HPV is integrated or replicating. The examiner cannot determine these limitations since the Office is not equipped to make such an evaluation. However, even if the limitations are not met by the reference it would have been obvious to meet the limitations for the following reasons. One in the art clearly knows that HPV is inhibited by antisense and also knows that conditions where cells are infected with HPV (a cervical intraepithelial neoplasia) contain integrated and non integrated and replicating and nonreplicating virus a various points of the diseases or conditions progression. It would be obvious to treat such a disease once it was detected, regardless of the state of the virus at any given moment. Clearly one would be motivated to start a treatment as soon as possible and for a duration of

sufficient length to eliminate as much virus as possible. Since the goal of treatment is to eliminate a virus 100% it would clearly be an optimization to eliminate a level (25, 50 or 75% on the road to total elimination. The invention as a whole, if not anticipated, would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

One in the art would have known that the topical application of siRNA was a mode of choice since the prior art has already shown the delivery of other nucleic acid drugs by this mode. One in the art would clearly have recognized also that any disease treatable by inhibiting HPV-16 would be treatable by siRNA as Crooke et al have at least identified by name cumulative types of neoplasia and carcinomas, for example.

Claims 21 and 22 are addressed with the following explanation.

The claimed invention is as is a method of inhibiting HPV-16 in cells in a mammal such as an immunodeficient mouse with human cells infected with HPV-16 therein. The references do not teach inhibiting HPV-16 in an experimental model [immunodeficient mice] as claimed. However it would be clearly obvious to use an established model such as nude or scid mice that have been used for xenograft experiments for decades. These models provide data for drug selection by enabling on in the art to test their drug in a growing tumor instead of in transformed cells in culture providing for more relevant study of the drug.

Since these models are well established tools for testing tumor drugs and antivirals and the claimed invention is for the treatment HPV infection and tumors [HPV

induced] it is clear that such an embodiment would have been obvious to one developing drugs for the treatment of HPV infection or induced tumors.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635

/Sean R McGarry/
Primary Examiner, Art Unit 1635